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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,576	08/09/2001	Carsten Andersen	10004.204-US	2881
25908	7590	12/08/2004	EXAMINER	
NOVOZYMES NORTH AMERICA, INC. 500 FIFTH AVENUE SUITE 1600 NEW YORK, NY 10110			RAO, MANJUNATH N	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 12/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/925,576

Applicant(s)

ANDERSEN ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-58 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-58 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>8-30-01</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 25-58 are currently pending and are present for examination.

Election/Restrictions

Applicant's apparent election of Group I drawn to variant amylase polypeptides in the reply filed on 9-21-04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Furthermore, Examiner also acknowledges the election of the species. Applicant was required to require a single species as opposed to the three species elected. Examiner warns that election to a single species will be imposed if applicants add on species during the prosecution of this application.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copies have been received.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable

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code (for example see page 32). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code throughout the specification. Examiner urges applicants to check the specification thoroughly for the recitation of the HTML language. See MPEP § 608.01. Appropriate correction is required.

Duplicate Claims, Warning

Applicant is advised that should claims 31, 38, 45, 52 be found allowable, claims 32, 39, 46 and 53 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 and claims 26-58 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 25 is drawn to a variant α -amylase comprising an alteration at specific amino acid positions which are selected from R118K, R320K or R458K and wherein the variant has at least 80% homology to an amino acid sequence selected from SEQ ID NO:2, 4, 6, etc. The claim as written suggests that the amino acids at positions 118, 320 and 458 are all 'R' which is changed to 'K' in the variant. It also

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suggests that all the SEQ ID NO included in the claim have 'R' at position 118, 320, 458.

However, a perusal of the sequence listing shows that it is not the case. The amino acids at the positions 118, 320 and 458 are not always 'R' as claimed. This has led to a confusion as to what is specifically claimed. A variant comprising 'K' at positions 118, 320, 458 irrespective of the amino acid at said positions or that the amino acid at said positions are always 'R' which is changed to 'K' in the variant. Because of this confusion and because of the fact that none of the sequences indicated in the claims have 'R' at the above positions it is impossible to do a thorough search. Correction/clarification is required. However, in order to expedite the prosecution Examiner has concluded that any amino acid sequence that is at least 80% identical to the SEQ ID NOs in claim 1 and having 'K' at any one of said positions reads on claim 1.

Claim 25 and claims 26-58 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 25 recites the phrase "using SEQ ID NO:12 for numbering" and is drawn to a variant to be derived from several other SEQ ID NO. It is not clear to the Examiner what applicants mean by the above phrase with respect to the large number of SEQ ID NO recited in the claim. It is not clear to the Examiner whether amino acid at position 118 in SEQ ID NO:2, 4, 6, etc. is the same as that in SEQ ID NO:12. By reciting the above phrase in the claim if applicants mean that the amino acid at position 118 in SEQ ID NO:2, 4, 6 etc. is not the same as the amino acid at position 118 of SEQ ID NO:12, then it will be impossible for the Examiner to determine the same and search the claims as written.

Applicant needs to clarify the above issue and make necessary corrections.

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Claims 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 26-29 recite the phrase "corresponding to". The metes and bounds of the above phrase is not clear to the Examiner. It is not clear to the Examiner whether the phrase, for example, "corresponding to R118K" means the amino acid is at position 118 in the claimed SEQ ID NO:2, 4, 6 etc. is an arginine which is changed to lysine or whether it refers to some other "arginine" amino acid at a different position which applicant claims as "corresponding to arginine at position 118". If it is the latter, then without a recitation in the claim as to which specific amino acid on SEQ ID NO:2, 4, 6 etc.. "corresponds to R118", it will be impossible for the Examiner to do a meaningful search. The same applies to other amino acid positions 320 and 458.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected because the invention appears to employ novel microorganisms.

Since the microorganisms are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public.

The claimed microorganisms are not fully disclosed, nor has it been shown to be publicly known and freely available. The specification does not disclose a repeatable process to obtain the microorganisms and it is not apparent if the microorganisms are readily available to the public. Accordingly, it is deemed that a deposit of these microorganisms should have been made in

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accordance with 37 CFR 1.801-1.809. In order for the claims to be enabled, applicants must show that either the microorganisms can be made by publicly available materials or that the microorganisms as such has been deposited in such a way that it is freely available to the public. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the microorganisms.

The deposits can be made in a recognized Biological Deposit Center. If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific plasmid/strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit is not made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;
2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
4. the deposit will be replaced if it should ever become inviable.

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It appears that some of the microorganisms have been deposited. However, it is not apparent whether they are freely available to the public.

Claims 25-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a variant amylase enzyme of SEQ ID NO:12 wherein the variant comprises an alteration selected from the group of alterations corresponding to amino acid at position 118, 320 or 458 and wherein the alteration specifically comprises replacing the amino acid at said positions with lysine (K), does not reasonably provide enablement for variant amylase enzyme wherein the variant comprises a polypeptide having at least 80%, 90%, 95% or 97% homology with SEQ ID NO:2, 4, 6, 8, 10, 12, or 13 as well as an alteration selected from the group of alterations corresponding to amino acid at position 118, 320 or 458 and wherein the alteration specifically comprises replacing the amino acid at said positions with lysine (K). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 25-58 are so broad as to encompass any amylase comprising the modifications at the above mentioned three positions and having 80% through 97% identity to SEQ ID NO:2, 4,

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6, 8, 10, 12, or 13. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of amylases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the variant amino acid sequence of only SEQ ID NO:12. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of SEQ ID NO: 12 with the any one of the three amino acid modifications as a amylase but provides no guidance with regard to the making of variants and mutants that are 80% to 97% identical to SEQ ID NO 2, 4, 6, 8, 10, 12, or 13 or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as

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encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any amylase with 80% through 97% identity to SEQ ID NO:2, 4, 6, 8, 10, 12, or 13 because the specification does not establish: (A) regions of the protein structure which may be modified without affecting amylase activity; (B) the general tolerance of amylases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including amylases with an enormous number of amino acid modifications to SEQ ID NOS: 2, 4, 6, 8, 10, 12, or 13. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is

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unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25, 27, 30, 31, 32, 36-39, 45-46, are rejected under 35 U.S.C. 102(b) as being anticipated by Igarashi et al. (Database SPTREMBL, Accession No. O82839, Nov. 1998). This rejection is based upon the public availability of an amino acid sequence. Claims 25, 27, 30, 31, 32, 36-39, 45-46 of the instant application are drawn to a variant amylase polypeptide wherein said variant has amino acid K corresponding to the position 320 and wherein said polypeptide is at least 80%, 90% or 95% identical to SEQ ID NO:2, 12, 13. Igarashi et al. disclose such an amylase polypeptide comprising the amino acid K at a position corresponding to 320 of SEQ ID NO:2, 12, and 13 (see enclosed sequence alignment). Therefore Igarashi et al. anticipate claims 25, 27, 30, 31, 32, 38-39, 45-46 of this application as written.

Conclusion

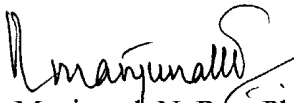
None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-

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0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

December 1, 2004